CLAIMS

1. A method of measuring methyl transferase activity of a polypeptide, said method comprising the steps of:

a. contacting a polypeptide selected from the group consisting of:

i. a polypeptide comprising the amino acid sequence of SEQ ID NO: 51 *(ZNFN3A1)*;

ii. a polypeptide comprising the amino acid sequence of SEQ ID NO: 51 wherein one or more amino acids are substituted, deleted, or inserted, and said polypeptide has a biological activity equivalent to the polypeptide consisting of the amino acid sequence of SEQ ID NO: 51;

iii. a polypeptide that comprises the amino acid sequence having at least about 80% homology to SEQ ID NO: 51; and

vi. a polypeptide encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of the nucleotide sequence of SEQ ID NO: 50, wherein the polypeptide has a biological activity equivalent to a polypeptide consisting of the amino acid sequence of SEQ ID NO: 51;

with a substrate to be methylated and a cofactor under the condition capable of methylation of the substrate;

b. detecting the methylation level of the substrate; and

c. measuring the methyl transferase activity by correlating the methylation level of step (b) with the methyl transferase activity.

2. The method of claim 1, wherein the substrate is a histone or the fragment thereof comprising an at least methylation region.

3. The method of claim 1, wherein the methylation region is a histone H3 lysine 4.

4. The method of claim 1, wherein the cofactor is a S-adenosyl-L-methyonine.

5. The method of claim 1, wherein the condition capable of methylation of the substrate is provided in the existence of heat shock protein 90A (HSP90A).

6. The method of claim 1, wherein the polypeptide is contacted with the substrate and cofactor in the presence of an enhancing agent for the methylation.

7. The method of claim 6, wherein the enhancing agent for the methylation is S-adenosyl homocysteine hydrolase (SAHH).

8. A method identifying an agent that modulate methyl transferase activity, said method comprising the steps of:
   a. contacting a polypeptide selected from the group consisting of:
      i. a polypeptide comprising the amino acid sequence of SEQ ID NO: 51;
      ii. a polypeptide that comprises the amino acid sequence of SEQ ID NO: 51 wherein one or more amino acids are substituted, deleted, or inserted, and said polypeptide has a biological activity equivalent to the polypeptide consisting of the amino acid sequence of SEQ ID NO: 51;
      iii. a polypeptide that comprises the amino acid sequence having at least about 80% homology to SEQ ID NO: 51; and
      vi.a polypeptide encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of the nucleotide sequence of SEQ ID NO: 50, wherein the polypeptide has a biological activity equivalent to a polypeptide consisting of the amino acid sequence of SEQ ID NO: 51;
   with a substrate to be methylated and a cofactor in the presence of the test compound under the condition capable of methylation of the substrate;
   b. detecting the methylation level of the substrate; and
   c. comparing the methylation level to a control level

   wherein an increase or decrease in the methylation level compared to control level indicates that the test compound modulates methyl transferase activity.

9. A kit for detecting for an activity of a test compound to regulate methyl transferase activity, said kit comprising the components of:
   a. a polypeptide selected from the group consisting of:
      i. a polypeptide comprising the amino acid sequence of SEQ ID NO: 51;
      ii. a polypeptide comprising the amino acid sequence of SEQ ID NO: 51 wherein one or more amino acids are substituted, deleted, or inserted and said polypeptide has a biological activity equivalent to the polypeptide consisting of the amino acid sequence of SEQ ID NO: 51;
      iii. a polypeptide that comprises the amino acid sequence having at least about 80% homology to SEQ ID NO: 51; and
      iv. a polypeptide encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of the nucleotide sequence of SEQ

ID NO: 50, wherein the polypeptide has a biological activity equivalent to a polypeptide consisting of the amino acid sequence of SEQ ID NO: 51;

b. a substrate capable of methylation by the polypeptide of (a),

c. a cofactor for the methylation of the substrate, and

d. HSP90A.

10. The kit of claim 9, wherein the substrate is a histone or the fragment thereof comprising an at least methylation region.

11. The kit of claim 9, wherein said kit further comprises the element of:

e. S-adenosyl homocysteine hydrolase (SAHH).

12 A method of screening for a compound for treating colorectal cancer or hepatocellular carcinoma, said method comprising the steps of:

a. identifying the compound having an activity to modulate methyl transferase activity by the method of claim 7, and

b. selecting a compound that decrease the methylation level of the substrate compared to a control level.

13. A method of screening for a compound for treating colorectal cancer or hepatocellular carcinoma, said method comprising the steps of:

a. contacting a polypeptide selected from the group consisting of:

i. a polypeptide comprising the amino acid sequence of SEQ ID NO: 51;

ii. a polypeptide comprising the amino acid sequence of SEQ ID NO: 51 wherein one or more amino acids are substituted, deleted, or inserted and said polypeptide has a biological activity equivalent to the polypeptide consisting of the amino acid sequence of SEQ ID NO: 51;

iii. a polypeptide that comprises the amino acid sequence having at least about 80% homology to SEQ ID NO: 51; and

vi. a polypeptide encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of the nucleotide sequence of SEQ ID NO: 50, wherein the polypeptide has a biological activity equivalent to a polypeptide consisting of the amino acid sequence of SEQ ID NO: 51;

with a heat shock protein 90A polypepetide (HSP90A) in the presence of a test compound;

b. detecting binding between the polypeptide and HSP90A;

c. comparing the binding of the polypeptide and HSP90A in the presence of the test compound with that in the absence of the test compound; and

d. selecting a test compound which decreases the binding of the polypeptide and HSP90A.

14. A kit for screening for a compound for treating colorectal cancer or hepatocellular carcinoma, said kit comprising the components of:

a. a polypeptide selected from the group consisting of:

i. a polypeptide comprising the amino acid sequence of SEQ ID NO: 51;

ii. a polypeptide comprising the amino acid sequence of SEQ ID NO: 51 wherein one or more amino acids are substituted, deleted, or inserted and said polypeptide has a biological activity equivalent to the polypeptide consisting of the amino acid sequence of SEQ ID NO: 51;

iii. a polypeptide that comprises the amino acid sequence having at least about 80% homology to SEQ ID NO: 51; and

vi. a polypeptide encoded by a polynucleotide that hybridizes under stringent conditions to a polynucleotide consisting of the nucleotide sequence of SEQ ID NO: 50, wherein the polypeptide has a biological activity equivalent to a polypeptide consisting of the amino acid sequence of SEQ ID NO: 51;

with a heat shock protein 90A polypepetide (HSP90A) in the presence of a test compound; and

b. HSP90A

15. A method of screening for a compound for treating colorectal cancer or hepatocellular carcinoma, said method comprising the steps of:

a. contacting a polypeptide comprising an contiguous amino acid sequence that selected from the amino acid sequence of SEQ ID NO: 51, and wherein the amino acid sequence comprises either or both of NHSCDPN (SEQ ID NO:52) and GEELTICY (SEQ ID NO:53), with an S-adenosyl-L-methyonine in the presence of a test compound;

b. detecting binding between the polypeptide and S-adenosyl-L-methyonine;

c. comparing the binding of the polypeptide and S-adenosyl-L-methyonine in the presence of the test compound with that in the absence of the test compound, and

d. selecting a test compound which decreases the binding of the polypeptide and S-adenosyl-L-methyonine.

16. A kit for screening for a compound for treating colorectal cancer or hepatocellular carcinoma, said kit comprising the components of:

a. a polypeptide comprising an contiguous amino acid sequence that selected from the amino acid sequence of SEQ ID NO: 51, and wherein the amino acid sequence comprises either or both of NHSCDPN (SEQ ID NO:52) and GEELTICY (SEQ ID NO:53); and

b. S-adenosyl-L-methyonine

17. A composition for alleviating a symptom of colorectal cancer or hepatocellular carcinoma, said composition comprising a pharmaceutically effective amount of a compound that decreases ZNFN3A1-mediated methylation and a pharmaceutically acceptable carrier.

18. A method for alleviating a symptom of colorectal cancer or hepatocellular carcinoma comprising contacting a colorectal cancer cell or a heptocellular carcinoma cell with a pharmaceutically effective amount of a compound that decreases ZNFN3A1-mediated methylation.

19. A method for alleviating a symptom of colorectal cancer or hepatocellular carcinoma comprising contacting a colorectal cancer cell or a heptocellular carcinoma cell with a pharmaceutically effective amount of a compound that decreases an interaction between ZNFN3A1 and HSP90A.

20. A method for alleviating a symptom of colorectal cancer or hepatocellular carcinoma comprising contacting a colorectal cancer cell or a heptocellular carcinoma cell with a pharmaceutically effective amount of a compound that decreases an interaction between ZNFN3A1 and S-adenosyl-L-methyonine.